

REMARKS

Claims 1-20 are pending in this application and are presented for examination.

Claim 1 stands rejected.

Reconsideration of the application is respectfully requested in view of the above claims and the following remarks. For the Examiner's convenience and reference, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action.

Applicants thank the Examiner for noting allowable subject matter in claims 19 and 20, as well as in claims 2-18, if rewritten in independent form.

Applicants believe no new matter is present in this or any other portion of the present amendment.

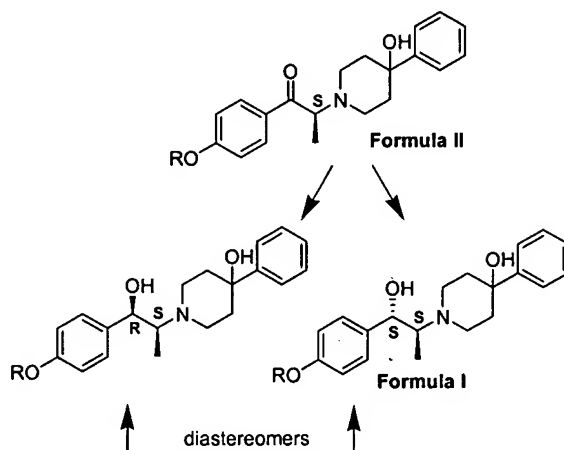
**I. Rejection under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph**

The Examiner has rejected claim 1 of the present application under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph as allegedly being indefinite. The Examiner alleges that "[c]ontrary to the structural formula, the claim defines the products being 'nonracemic diastereomer' of formula I and 'stereoisomers' thereof, i.e. are they nonracemic diastereomer only? Are they including other stereoisomers? Or are they inclusive of all the compounds embraced by the structural formula I?" Applicants respectfully traverse the rejection.

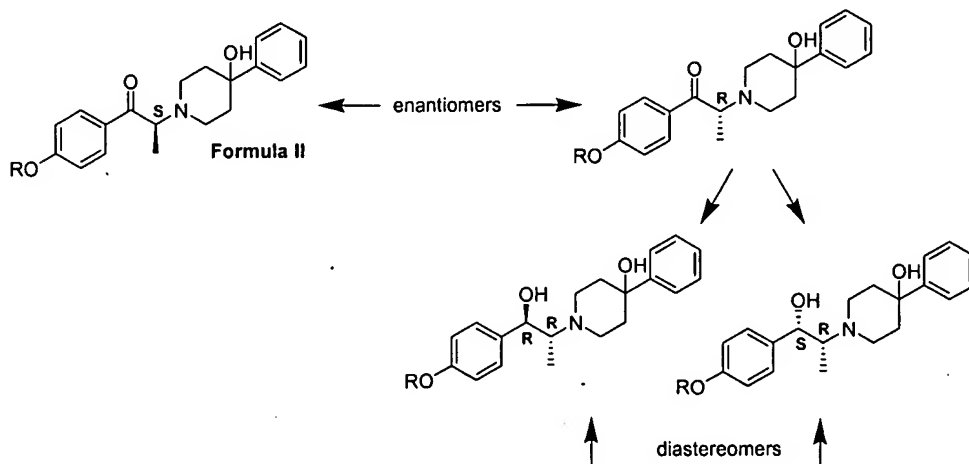
In the introductory organic chemistry textbook "Organic Chemistry", 3<sup>rd</sup> ed., John McMurry, **stereoisomer** is defined as isomers that have their atoms connected in the same order but have different three-dimensional arrangements. The term stereoisomer includes both enantiomers and diastereomers. In the same textbook, **diastereomer** is defined as a term that indicates the relationship between non-mirror-image stereoisomers that have the same configuration at one or more stereogenic centers, but differ at other stereogenic centers. McMurry also defines **enantiomers** as stereoisomers of a chiral substance that have a mirror-

image relationship. Enantiomers must have opposite configurations at all stereogenic centers in the molecule.

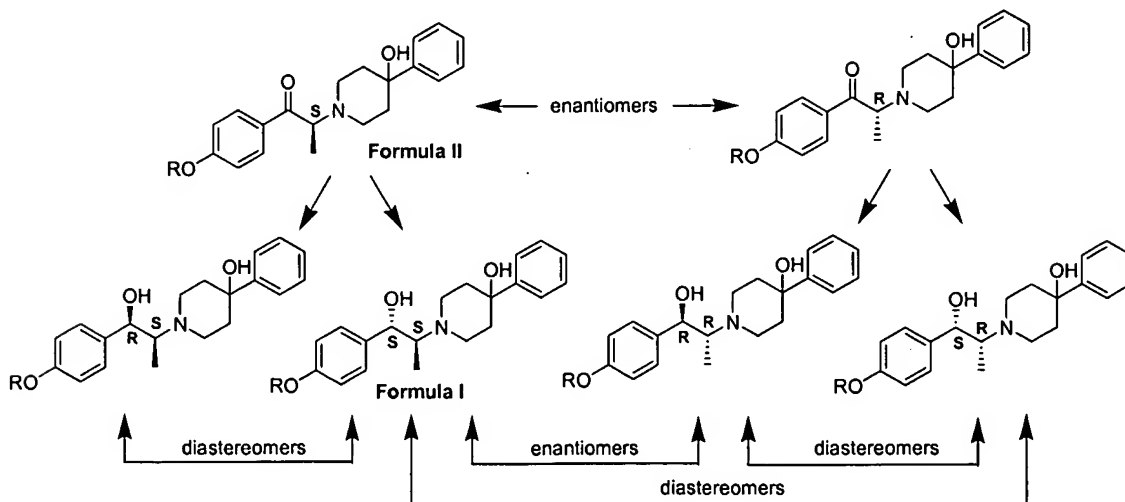
The present invention relates to the preparation of a nonracemic diastereomer of formula I, starting from a single enantiomer of formula II, as shown below. Starting with the (S) isomer, the process of the present invention can make either the (1R,2S) or the (1S,2S) diastereomer, depending on the choice of catalyst, diphosphine ligand, amine ligand, and base. As is clear from the scheme below, the stereochemistry of the  $\alpha$ -carbon does not change, it remains in the (S) configuration. Only the stereochemistry at the carbonyl carbon changes (R or S), depending on the catalyst mixture used. As the two possible compounds have one stereogenic center that is the same, and another that is different, the two possible products are defined as diastereomers of each other.



Starting with the other enantiomer of formula II, the (R) isomer, the process of the present invention can make either the (1R,2R) or the (1S,2R) diastereomer, as shown below.



Like the possible products for the (S) isomer of formula II shown previously, the possible products of the (R) isomer of formula II have one stereogenic center that is the same (2R), and another that is different (1S vs. 1R), thus, the two possible products are defined as diastereomers of each other. In this manner, it is possible to selectively prepare all four possible *stereoisomers* of formula I (the (1R,2S), (1S,2S), (1R,2R) and (1S,2R)), starting from the two enantiomers of formula II:



As can be seen above, the (1R,2S) stereoisomer is a diastereomer of formula I (1S,2S), the (1R,2R) stereoisomer is an enantiomer, and the (1S,2R) stereoisomer is a diastereomer. Clearly,

as all the stereoisomers of formula I are diastereomers of each other, all are included in the scope of the claims. Accordingly, Applicants respectfully submit that there is nothing contrary between the claim language and the structure of formula I. As such, Applicants respectfully request that the rejection be withdrawn.

## **II. Rejection under 35 U.S.C. § 112, 1<sup>st</sup> paragraph**

The Examiner has further rejected claim 1 of the present application under 35 U.S.C. § 112, 1<sup>st</sup> paragraph as allegedly lacking enablement. The Examiner alleges that “[i]f the products being made are all stereoisomers of the structural formula instead of the *syn*-enantiomer as described on page 7 of the specification, then, critical or essential steps to the process as to how to obtain each nonracemic enantiomer without separation are lacking and must be incorporated into the claim.” Applicants respectfully traverse the rejection.

As described above, starting with the (S) enantiomer of formula II, the process of the present invention can yield either the (1R,2S) or the (1S,2S) diastereomers. Which one is produced depends on the particular mixture of the catalyst, diphosphine ligand, amine ligand and base. Likewise, starting with the (R) enantiomer of formula II, the process of the present invention can yield either the (1R,2R) or the (1S,2R) diastereomers. Again, which one is produced depends on the particular mixture of the catalyst, diphosphine ligand, amine ligand and base.

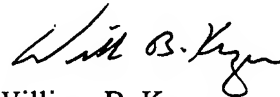
As examples 1-27 show, both the *syn*-enantiomers (1R,2R) and (1S,2S), as well as the *anti*-enantiomers (1R,2S) and (1S,2R) can be prepared individually and directly from the appropriate enantiomer of formula II using the appropriate catalyst, ligands, and base. Accordingly, no additional separation steps are required, since each stereoisomer is prepared with very high diastereomeric excess. As such, Applicants submit that the rejection is moot and request that the rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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